

Claims

What is claimed is:

1. An absorbable polyester with at least one monophosphate functionality per absorbable polyester chain.

2. A conjugate comprising an absorbable polyester according to claim 1 and a peptide and/or a bioactive agent, where the peptide and bioactive agent have at least one interactive amino group, wherein the monophosphate functionality forms a linkage with the amino group.

3. A conjugate according to claim 2 wherein the peptide is selected from the group consisting of p-Glu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH₂, H-β-D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, N-hydroxyethylpiperazinyl-acetyl-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond and N-hydroxyethylpiperazinyl-ethylsulfonyl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, or a pharmaceutically acceptable salt thereof.

4. A solid absorbable microparticle which comprises the absorbable polyester according to claim 1 and having a surface, wherein more than one percent of the monophosphate functionality resides on the surface of the absorbable microparticle.

5. A conjugate comprising the absorbable microparticle according to claim 4 and a peptide and/or a bioactive agent, where the peptide and bioactive agent have at least one interactive amino group, wherein the monophosphate functionality on the surface of the absorbable microparticle forms a linkage with the amino group.

6. A conjugate according to claim 5 wherein the peptide is selected from the group consisting of p-Glu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH₂, H-β-D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, N-hydroxyethylpiperazinyl-acetyl-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond and N-hydroxyethylpiperazinyl-ethylsulfonyl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, or a pharmaceutically acceptable salt thereof.

7. An acylated or alkylated absorbable polysaccharide, having one or more terminal monophosphate functionality per molecule.

8. An acylated or alkylated absorbable polysaccharide according to claim 7 wherein said absorbable polysaccharide is an acylated gamma-cyclodextrin.

9. A conjugate comprising the alkylated or acylated absorbable polysaccharide according to claim 7 and a peptide and/or a bioactive agent, where the peptide and bioactive agent have at least one interactive amino group, wherein the monophosphate functionality forms a linkage with the amino group.

- 5 10. A conjugate according to claim 9 wherein the peptide is selected from the group consisting of p-Glu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH₂, H-β-D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, N-hydroxyethylpiperazinyl-acetyl-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond and N-hydroxyethylpiperazinyl-ethylsulfonyl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond,
10 or a pharmaceutically acceptable salt thereof.

11. An absorbable polyester according to claim 1, wherein the polyester chain comprises one or more monomers selected from the group consisting of L-lactic acid, D-lactic acid, DL-lactic acid, malic acid, citric acid, tartaric acid, ε-caprolactone, ε-caproic
15 acid, alkylene oxalate, cycloalkylene oxalate, alkylene succinate, β-hydroxybutyrate, glycolide, glycolic acid, L-lactide, D-lactide, DL-lactide, meso-lactide, trimethylene carbonate, p-dioxanone, 1,5-dioxepan-2-one and 1,4-dioxepan-2-one and any optically active isomers, racemates, or copolymers thereof.

12. An absorbable polyester according to claim 11 further comprising one or
20 more polyethylene glycol segments covalently linked to said polyester.

13. A conjugate comprising an absorbable polyester according to claim 12 and a peptide and/or a bioactive agent, where the peptide and bioactive agent have at least one interactive amino group, wherein the monophosphate functionality forms a linkage with the amino group.

- 25 14. A conjugate according to claim 13 wherein the peptide is selected from the group consisting of p-Glu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH₂, H-β-D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond, N-hydroxyethylpiperazinyl-acetyl-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond and N-hydroxyethylpiperazinyl-ethylsulfonyl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ where the two Cys are bonded by a disulfide bond,
30 or a pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition comprising a conjugate according to claim 2 and a pharmaceutically acceptable carrier.

16. A pharmaceutical composition comprising a conjugate according to claim 5 and a pharmaceutically acceptable carrier.

17. A pharmaceutical composition comprising a conjugate according to claim 9 and a pharmaceutically acceptable carrier.

5 18. A pharmaceutical composition comprising a conjugate according to claim 13 and a pharmaceutically acceptable carrier.

19. An absorbable polymer according to claim 1 for use as an acidic excipient of a cyanoacrylate composition.

10 20. A method for making a low melting phosphorylated-hydroxyl-bearing polyester having 1% to 60% crystallinity, which comprises reacting a hydroxyl-bearing polyester with an excess of pyrophosphoric acid to yield the phosphorylated-hydroxyl-bearing polyester.

15 21. A method for making a phosphorylated-acylated cyclodextrin, which comprises reacting an acylated cyclodextrin with an excess of pyrophosphoric acid to yield the phosphorylated-acylated cyclodextrin.

22. A method for making a phosphorylated-alkylated cyclodextrin, which comprises reacting an alkylated cyclodextrin with an excess of pyrophosphoric acid to yield the phosphorylated-alkylated cyclodextrin.

20 23. A method for making phosphorylated microparticles, which comprises reacting a hydroxyl-bearing microparticle with excess pyrophosphoric acid to yield the phosphorylated microparticles.

25 24. A method of making an acylated-phosphorylated polysaccharide, which comprises reacting a polysaccharide concurrently with a heated mixture of pyrophosphoric acid and an acylating agent to yield the acylated-phosphorylated polysaccharide.

25. A method according to claim 24, wherein the polysaccharide is cyclodextrin and the acylating agent is propionic anhydride or acetic anhydride.

26. A phosphorylated-grafted-acylated cyclodextrin having one or more monophosphate functionality.

30 27. A method of preparing phosphorylated-grafted-acylated cyclodextrin, which comprises heating a monomer with an acylated cyclodextrin in the presence of a catalytic amount of stannous octoate for about 2-24 hours at about 100 °C to 200 °C to form a reaction mixture comprising grafted-acylated cyclodextrin; dissolving the reaction

